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Effect of birth mode on IL-17 receptor expression in cord blood-derived CD4+ T lymphocytes

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Abstract

Aim: The Interleukin 17 (IL-17) family of cytokines plays a crucial role in host defense against microorganisms and the development of inflammatory diseases. The IL-17 receptor family, consisting of IL-17RA, IL-17RB, IL-17RC, IL-17RD, and IL-17RE, is central to the IL-17 signaling pathway. Emerging evidence suggests that birth mode might influence the development of the immune system and the risk of immune-related disorders. This study aimed to investigate the potential effect of birth mode on the expression of IL-17 receptor family members (IL-17RA, IL-17RB, and IL-17RC) in cord blood-derived CD4+ T lymphocytes.

Material and Methods: Cord blood samples were collected from volunteer pregnant women who had either vaginal deliveries or cesarean sections (n=20 each). Mononuclear cells were isolated, and CD4+ T lymphocytes were analyzed for the expression of IL-17 receptor family members using flow cytometry. Mean fluorescence intensity (MFI) was used to quantify receptor expression levels.

Results: The expression level of IL-17RA was significantly higher in the vaginal delivery group compared to the cesarean section group ($p<0.05$). However, there was no significant difference in the expression levels of IL-17RB and IL-17RC between the two groups.

Discussion: The findings of this study suggest that birth mode might have an impact on the expression of IL-17 receptor family members in cord blood-derived CD4+ T lymphocytes. Notably, IL-17RA expression was notably higher in infants born through vaginal delivery, indicating a potential role of birth mode in shaping immune system development. This study provides novel insights into the potential association between birth mode and IL-17 receptor expression in cord blood-derived CD4+ T lymphocytes. The observed differences in IL-17 receptor expression levels highlight the need for further research to elucidate the mechanisms underlying the interaction between birth mode and immune system development.

Keywords

IL-17 Receptors, Birth Mode, Cord Blood, CD4+ T Lymphocytes, Cord Blood

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Introduction

The Interleukin 17 (IL-17) family is an important cytokine family involved in host defense against microorganisms and the development of inflammatory diseases. The IL-17 receptor family consists of five members (IL-17RA, RB, RC, RD, and RE), each of which shares a series of homologies with their ligands [1]. Studies comparing the impact of birth mode, an important factor in neonatal immune system development, have been conducted in different geographic locations. Particularly, the cesarean section delivery is highlighted for its potential to disrupt the transmission of the maternal microbiome and jeopardize infant intestinal microbiome programming [2-3]. It has been shown that this condition negatively affects immunological development and increases the risk of allergic diseases [4]. Cord blood (CB) is widely used as an alternative source of hematopoietic stem cells for diseases requiring hematopoietic stem cell transplantation (HSCT). Cord blood collection, storage under laboratory conditions, and release when needed are routinely applied. Cord blood banking can be performed autologously and allogeneically in Turkey, known as the 'Turkish Model'. In a previous study conducted by our group, the release rate for clinical use was found to be between 0.41% and 0.99% [5]. This rate varies worldwide, and many banks do not publish their release rates [6]. In recent years, cord blood has also been preferred as a source of mesenchymal stem cells with potential applications in regenerative and reparative medicine [7]. Additionally, studies on lymphocyte subsets derived from cord blood for cellular immunotherapy are ongoing [8]. The aim of this study is to compare the expression levels of IL-17 receptor family members IL17RA, IL17RB, and IL17RC in CD4+ lymphocytes isolated from cord blood obtained from individuals who had vaginal or cesarean section deliveries. The aim of the study is to evaluate the potential impact of birth mode, which is believed to play a role in immunological development, on IL17 receptor expression.

Material and Methods

Cord blood samples obtained from pregnant volunteers who gave birth within the stipulated timeframe, in accordance with the Ministry of Health's Cord Blood Banking Regulation (Official Gazette Date:05.07.2005 Official Gazette Number:25866), were subjected to cellular and microbiological quality control tests as stipulated by relevant regulations. For this purpose, leftover cord blood samples from 2 ml EDTA-containing specimen samples were utilized for immunophenotypic analyses. Additional sampling was not performed in this study. Expression levels of IL17RA (R&D Human IL-17RA/IL-17R APC-conjugated Antibody FAB177A), IL17RB (BD Pharmingen™ Alexa Fluor® 647 Rat Anti-Mouse IL-17 Receptor B Cat No:565866), and IL17RC (Human IL-17RC Alexa Fluor® 647-conjugated Antibody Catalog #: FAB22691) were evaluated by flow cytometry in mononuclear cells isolated from cord blood obtained from volunteer pregnant women (n=20) who consented to participate in the study. After immunophenotyping, lymphocytes were gated in the FSC/SSC histogram, and CD4+CD3+ cells were analyzed for IL17 receptor expression. Expression levels were calculated as mean fluorescence intensity (MFI). Statistical analysis was conducted using SPSS 21 program. The Mann-Whitney U test was used for group comparisons, and p<0.05 was considered significant. The study was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee on 06-12-2017 with decision No. 712.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

While the expression level of IL17RA was significantly higher in the vaginal delivery group compared to the cesarean group (P<0.05), no difference was detected in IL17RB and IL17RC expressions (Table 1, Figures 1, 2).

Table 1. IL-17 Receptor expression levels in vaginal delivery and cesarean groups. SD: standard deviation, IL17RA: interleukin 17 receptor A, IL17RB: interleukin receptor B, IL17RC: interleukin 17 receptor C, S/C:Section.

		N	Mean	SD	Min.	Max.	p
IL17RA	VAGİNAL DELİVERY	10	129,3	3,69	114	144	0,001
	S/C	10	100,9	0,75	98	105	
IL17RB	VAGİNAL DELİVERY	10	100,3	0,59	98	105	0,844
	S/C	10	100,5	0,8	97	104	
IL17RC	VAGİNAL DELİVERY	10	109,5	0,88	106	114	0,603
	S/C	10	108,9	0,7	106	113	

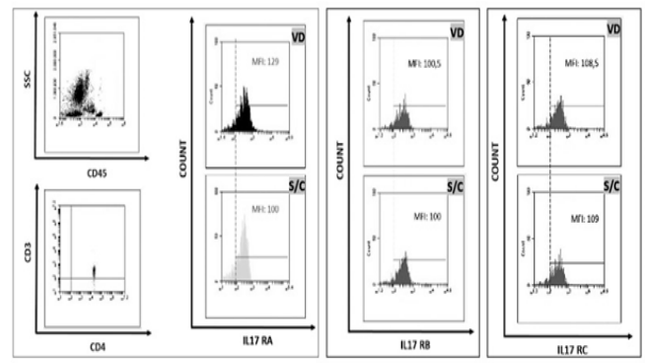

Figure 1. Histogram images of IL17RA, IL17RB, and IL17RC expression levels by flow cytometry. After gating CD45 positive lymphocytes, CD3+CD4+ cells were gated. Then, IL17RA, IL17RB, and IL17RC expression levels were evaluated in CD45+CD3+CD4+ cells as mean fluorescence intensity (MFI). VD: Vaginal Delivery, S/C:Section.

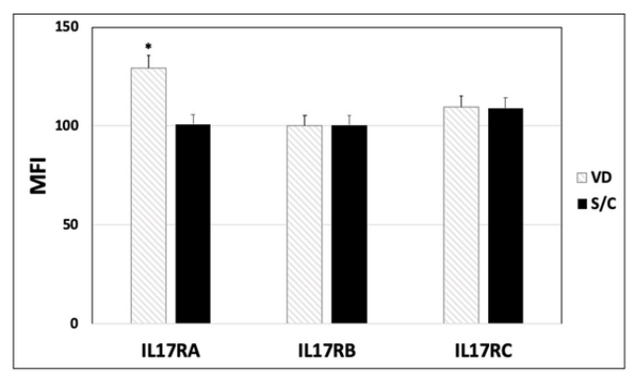

Figure 2. IL17RA, IL17RB, and IL17RC expression levels. *P<0.05, MFI: mean fluorescence intensity, VD: Vaginal Delivery, S/C: Section.

Discussion

This study was conducted to reveal the effect of birth mode on IL-17 receptor family members for the first time. Our findings emphasize the potential influence of birth mode on this cytokine family by showing significantly higher IL17RA expression in the vaginal delivery group compared to the cesarean group. This result can be considered an important step in better understanding the impact of birth mode on immune system development, disease pathophysiology, and allergic diseases. These findings could contribute to future health strategies by helping us understand the effects of birth on the immune system. Interestingly, the lack of an effect of birth mode on IL17RB and IL17RC expression levels might suggest that these receptors could have a less determining role in immunological development. However, these results need further support through additional research. Detailed studies on the activation and signaling pathways of IL-17 receptor family members could help us better understand their specific roles and functions. Different subsets of lymphocytes, especially T cells and natural killer cells, derived from cord blood have been shown to play an important role in immune system development and regulation [8-9]. Therefore, cell-based therapies using these subsets hold potential for future cancer immunotherapy and the treatment of other immunological diseases [10-11]. This new information allows us to assess the effects of different cell types present in cord blood on the immune system in a broader context. Our findings could offer a more comprehensive understanding of the interactions between these cell types and immune system regulation, taking into consideration the differences that could arise from factors such as genetics and environmental influences.

Conclusion

This study has taken an important step in examining the effects of normal vaginal delivery and cesarean section on the expression levels of IL-17 receptor family members. Our findings, by showing increased IL17RA expression in vaginal delivery, demonstrate the potential influence of birth mode on immune system development. However, the limitations of this study should also be considered. The sample size was limited, and the focus was on cord blood samples only. Future studies should examine the effects of different birth modes on immune development more comprehensively, using larger and more diverse sample groups. In conclusion, this study examining the expression levels of IL-17 receptor family members based on birth mode could contribute to a better understanding of immune system development and diseases.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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